

REMARKS

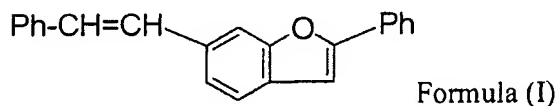
Claims 1-2 and 5-17 are pending and have been examined on the merits. Claims 5-10 and 12-17 are withdrawn from consideration and claims 1 and 2 are amended hereinabove. Claim 1 has been amended: (a) to show the group R_{10} in position 3 of the benzofurane ring, (b) to introduce the feature "wherein at least one of R_8 , R_9 and R_{10} is OPO_3H_2 or $OCH_2OPO_3H_2$, and their disodium salt", and (c) to better define the invention. Claim 2 has been amended to reflect the limitations introduced on claim 1. No new matter has been added.

In the Office Action, the claims have been rejected as follows:

- a) Claims 1 and 11 stand rejected under 35 U.S.C. § 102(b), as being anticipated by Siegrist (U.S. Patent No. 3,697,513, hereinafter "Siegrist");
- b) Claims 1 and 11 stand rejected under 35 U.S.C. § 103(a) as being obvious over Kawai et al. (U.S. Patent No. 5,858,995, hereinafter "Kawai");
- c) Claim 2 is objected to as allegedly reading on non-elected subject matter.

Applicants respectfully traverse these rejections.

Siegrist teaches a compound of formula (I):



However, the currently amended claim 1 now recites that at least one of R_8 , R_9 and R_{10} is OPO_3H_2 or $OCH_2OPO_3H_2$ and their disodium salt. Accordingly, it is respectfully submitted that the combination of " R_8 and R_9 being H and R_{10} being C_6H_5 " can no longer occur and therefore Siegrist does not teach all of the claim's limitations as reported in the

Office Action of August 8, 2008, page 4, paragraph 5. Accordingly, the withdrawal of the rejection of claims 1 and 11 as being anticipated by Siegrist under 35 U.S.C. § 102(b) is respectfully requested.

As set forth above, amended claim 1 now recites the features of the mandatory presence of at least a phosphate group, such that at least one of R_8 , R_9 and R_{10} is OPO_3H_2 or $OCH_2OPO_3H_2$ and their disodium salt.

Kawai teaches a formula (I) in which R^1 corresponds to the presently claimed R_8 and R_9 (*e.g.*, col. 1, lines 57-59), and R^2 and R^3 correspond to the presently claimed R_{10} (*e.g.*, from col. 1 line 60, to col. 2 line 18). As such, Kawai does not disclose, teach or even suggest the presence of at least one phosphate group on the benzofuran moiety nor does it suggest any role for the phosphate groups.

On the other hand, the claimed compounds ST2496 represent an improvement over the prior art, in that they solve a drawback of the combretastatins already known in the art. That is, combretastatin A4 has a dose limiting toxicity reportedly known to cause acute coronary syndrome (*e.g.*, specification page 57). On the contrary, the elected species ST2496 does not induce significant changes on blood pressure and heart rate. It is submitted that this additional technical feature of lacking cardiovascular side effects is believed to be due to the presence of phosphate group in positions 4, 5 or 7 on the ST2496 molecule.

Accordingly, a person skilled in the art would not find any motivation in Kawai to add phosphate groups to the compounds disclosed therein. There is nothing on record to indicate that such modification of Kawai would be desirable or even suggested to one of

ordinary skill. It is respectfully submitted that the Examiner has used impermissible hindsight to reach that conclusion after reading Applicants' disclosure.

In addition, Applicants respectfully disagree with the Examiner's statement on page 4 of the Office Action that Kawai's compounds are useful for treating bone cancer. It is submitted that Kawai is completely silent with regard on how to use its compounds, let alone on how to treat bone cancer. The simple fact of mentioning that the unrelated Kawai's compounds can be used to treat bone metastasis does not render the reference enabling as to the claimed compounds. The intended purpose of unrelated compounds is not relevant to determine whether the claimed compounds containing the phosphorus groups are patentable.

Moreover, the standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied.

Accordingly, it is submitted that simply listing potential applications for a class of compounds does not meet the above-mentioned standard if nothing more is disclosed because the needed experimentation would be undue and unreasonable. As such, for the reason set forth above, it is submitted that Kawai is not even enabling with regard of bone cancer treatments.

Thus, for this additional reason, Kawai does not provide a motivation to one skilled in the art to modify the compounds disclosed therein to arrive at the presently claimed invention.

Accordingly, withdrawal of the rejection of claims 1 and 11 as being obvious over Kawai under 35 U.S.C. § 103(a) is respectfully requested.

Finally, it is submitted that the amendment to claim 2 overcomes its objection for allegedly being directed to non-elected subject matter.

Thus, it is submitted that all of the pending claims are now in conditions for allowance and a Notice to that effect is earnestly solicited.

This response is being filed within the shortened statutory period for response, thus, no fees are believed to be due. If, on the other hand, it is determined that further fees are necessary or any overpayment has been made, the Commissioner is hereby authorized to debit or credit such sum to Deposit Account No. 02-2275.

Pursuant to 37 C.F.R. § 1.136(a), please treat this and any concurrent or future reply in this application that requires a petition for an extension of time of its timely submission as incorporating a petition for extension of time for the appropriate length of time. The fee associated herewith is to be charged to the above-mentioned deposit account.

An early and favorable action on the merits is earnestly solicited.

Respectfully submitted

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